II. REMARKS

Preliminary Remarks

Reconsideration and allowance of the present application based on the following remarks and foregoing amendment are respectfully requested. Claims 24-26 have been allowed. Claims 20, 21, and 27-39 remain at issue.

The applicants have amended claim 20 to remove the term "bacterium" for clarity and not for any reasons related to patentability. New claims 40 and 41 are directed to a recombinant *C. glutamicum* comprising a *C. glutamicum* nucleic acid consisting of SEQ ID NOS: 1 or 2 or a fragment thereof, and encoding a polypeptide that enhances amylase secretion. New claims 42 and 43 are directed to vector and host cells comprising the nucleic acid molecules of claims 40 and 41. Support for new claims 40-43 can be found throughout the specification for example, page 6, lines 10-20, originally filed claims 8 and 9 and Examples 4-6.

The applicants do not intend by these or any amendments to abandon subject matter of the claims as originally filed or later presented, and reserve the right to pursue such subject matter in continuing applications.

Rejection Pursuant to 35 U.S.C. §101, first paragraph

In paragraph 2 of the official action, the examiner rejected claims 20, 30 and 32-39 under 35 U.S.C. § 112, first paragraph, for lack of enablement. Specifically, the examiner alleged that while the specification is enabling for an isolated polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:3, an isolated polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:4, a vector comprising said polynucleotide, and a recombinant *Corynebacterium glutamicum* comprising said polynucleotide, the specification does not reasonably provide enablement for any other embodiment. The examiner further asserted the specification does not provide guidance with respect to the specific structural/catalytic amino acids and the structural motifs essential for protein/enzyme structure and activity. The examiner further alleged that searching for specific nucleotides to change (deletion, insertion, substitution, or combinations thereof) in a polynucleotide is outside the realm of routine experimentation and predictability in

determining whether the resulting polypeptide as activity. Accordingly, the examiner concluded that one skilled in the art would require additional guidance, such as information regarding the specific catalytic amino acids and the structural motifs essential for activity/function which must be preserved.

The issue of enablement involves the question of whether an application enables one of ordinary skill in the art to make and to use the claimed invention. Clearly, the specification teaches that overexpression of the *sec*D (polynucleotide sequence SEQ ID NO: 1; amino acid sequence SEQ ID NO: 3) and *sec*F (polynucleotide sequence SEQ ID NO: 2; amino acid sequence SEQ ID NO: 4) genes enhance the secretion of the heterologously expressed amylase protein in *Corynebacterium glutamicum* (line 12, page 23, to line 28, page 24). Example 8 teaches the overexpression of *sec*D and *sec*F enhances the amylase secretion 1.5 fold in *C. glutamicum* (page 23, lines 26 and 27). When the *sec* genes *sec*D and *sec*F are combined with *sec* genes *sec*E and *sec*Y, the amylase secretion increases 2 to 3 fold in *C. glutamicum*. The term "functional mutants" is defined by the specification as those proteins with an amino acid sequence according to SEQ ID NOS: 3 and 4, whereby a single or several amino acids are artificially or naturally replaced by amino acids with different properties, however, the protein as a whole shows similar characteristics concerning functional behavior or effectiveness in the embodiment of enhancing amylase secretion (see page 6, lines 1-9). Therefore, it is the applicants' position that a functional mutant that enhances amylase secretion requires knowledge or teachings of the important conserved regions of the *C. glutamicum* SecD and SecF proteins. The applicants submit their teachings accomplish requirement.

Undue experimentation would not be required to enhance amylase secretion by using functional mutants of the encode SecD and SecF proteins. Claim 20 satisfies the "how to make prong" of the enablement requirement because the scope of the claims is "reasonably correlated" with the teachings of the application [See MPEP §2164.04(b)]. The present specification and the ordinary skill in the art permit one to identify the important regions of the *sec*D and *sec*F genes. The present specification specifically defines the homologous amino acid sequences and the functional mutants from line 26, page 5 to line 9, page 6 of *sec*D. The applicants also teach the *C. glutamicum* SecD protein possesses six putative transmembrane spanning regions in an unregular distribution with an extracytoplasmatic loop of 371 residues and six conserved motifs D1-D6. The deduced amino acid sequence of the

*sec*D gene is 61% similar to the *M. tuberculosis* gene, and are highly conserved over the transmembrane and the 6 short motifs D1-D6 (see line 21, page 3 to line 24, page 4).

The *C. glutamicum* SecF protein also has six transmembrane spanning regions and an extracytoplasmic loop of 95 residues which are highly conserved with the deduced amino acid sequence of the M. tuberculosis gene (see page 4, line 25 to page 5, line 14). Example 6 teaches how the amylase activity assays were performed and how the results were correlated with the enhanced export activities of the SecD and SecF proteins. Accordingly, it is the applicants' position that one of skill in the art would not require undue experimentation to identify specific catalytic amino acids and structural motifs essential for the enhanced export of amylase via the SecD and SecF proteins. Accordingly, due to teachings of the specification and what was known in the art at the time of filing, the experimentation necessary to practice the present invention would not be undue.

Claims 30, and 32-39 are dependent upon claims 20 and 24 and thus drawn the same limitations. In view of the foregoing remarks, the applicants respectfully submit the rejection of claims 20, 30, and 32-39 under 35 U.S.C. §112, first paragraph, for lacking enablement has been overcome and should be withdrawn.

Rejection Pursuant to 35 U.S.C. §112, Second Paragraph

In paragraph 4 of the official action, the examiner rejected claims 27-29 and 31-39 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the examiner alleged that the phrase "SEQ ID NO: 1 nucleotides 34 to 1944" and the phrase "SEQ ID NO: 2 nucleotides 22 to 1230" render claims 27-29 vague and indefinite because the meaning of the phrase is not known and not defined in the specification.

Amended claim 27 is now directed to a recombinant *Corynebacterium glutamicum* bacterium comprising at least one *Corynebacterium glutamicum* polynucleotide selected from the group consisting of (a) an isolated polynucleotide comprising nucleotides 34 to 1944 of SEQ ID NO:1 and (b) an isolated polynucleotide comprising nucleotides 22 to 1230 of SEQ ID NO:2. Amended claims 28 and 29 are directed to the bacterium of claim 27, wherein said isolated polynucleotide comprising nucleotides 34 to 1944 of SEQ ID NO: 1 or nucleotides 22 to 1230 of SEQ ID NO: 2 encodes a polypeptide that enhances excretion of an amylase

from the cytoplasm of said bacterium to a broth. The applicants submit amended claims 27-29 reflect the phrasing suggested by the examiner for which the applicants are grateful. In view of the foregoing amendment, the applicants respectfully submit the rejection of claims 27-29 and 31-39 under the 35 U.S.C §112, second paragraph has been overcome and should be withdrawn.

Rejection Pursuant to 35 U.S.C. 103(a)

In paragraph 7 of the official action, the examiner rejected claims 21, 30 and 32 under 35 U.S.C. § 103(a), as being unpatentable over Billman-Jacobe *et al.*, *Applied and Environmental Microbiology* 60:1641-1645 (1994) in view of the combined teaching of Smith (U00011) and Van Mellaert *et al.*, *Recent Research Developments in Microbiology* 3: 425-440 (1999).

Solely to expedite prosecution and without prejudice to the applicants' right to seek broader claims without prejudice to the applicants' right to seek broader claims in a continuing application, claim 21 has been canceled without prejudice thereby obviating the rejection of this claim. Dependent claims 30 and 32 are no longer dependent upon claim 21 and thus the rejection of these claims is moot as well. In view of the foregoing amendment, the applicants respectfully submit the rejection of claims 21, 30, and 32 under 35 U.S.C. §103(a) as being unpatentable over Billman-Jacobe *et al.* in view of Smith and Van Mellaert is moot and should be withdrawn.

III. CONCLUSION

In view of the foregoing, the claims are now believed to be in form for allowance, and such action is hereby solicited. If any point remains in issue which the Examiner feels may be best resolved through a personal or telephone interview, please contact the undersigned at the telephone number listed below.

Respectfully submitted,

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